THE WALTER AND ELIZA HALL INSTITUTE OF RESEARCH IN PATHOLOGY AND MEDICINE

THE DIRECTOR'S SEVENTEENTH ANNUAL REPORT 1935-36

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Historical Preface

The Walter and Eliza Hall Institute of Research in Pathology and Medicine was founded in 1916. The Trustees of the late Walter and Eliza Hall completed the Pathological Block of the present Royal Melbourne Hospital, and provided an annual payment of £2,500 towards the upkeep of the Institute. In 1925 this was increased to £3,100, and since 1930 has been £3,200 annually. In addition, the Institute has received, since its inception, £500 per annum from the University, the Medical Staff of the Melbourne Hospital having agreed that this portion of its clinical fund should be so used. Since 1925 a further sum of £250 per annum has been provided by the University from interest on the Appeal Fund (1924), together with an annual contribution from the Clinical Research Fund.

In 1926 the late Sir Aaron Danks, then President of the Melbourne Hospital, established an Endowment Fund to support a Bio-chemical Department. This fund has now reached the total of £8,591. The Edward Wilson Trustees maintained this new department by contributing £1,500 per annum in 1926, 1927 and 1928, and £1,000 in 1929. This Trust also, in 1926, contributed £3,000 for the foundation of an Institute Library, and of this sum £2,000 has been invested as endowment.

Since 1928 the Institute has been supported also by an annual contribution of £300 from the Felton Bequest Committee, and since 1933 by a contribution of £100 per annum from the Trustees of the late Anthony Mackie. The Trustees of the late T. J. Sumner have also helped to support the Institute since 1929.

The Institute has also received substantial support from the Department of Health of the Commonwealth Government; in the years 1927, 1928, 1929, 1930 and 1931 a total of £10,650 was received for special researches. In 1934 the Commonwealth Government entered into an agreement with the Rockefeller Foundation that each would contribute to the Institute the sum of £1,000 per annum for the ensuing three years to support work on Virus diseases, particularly those affecting the central nervous system.

1932, by the will of the late Mrs. L. E. W. Carty, of Brisbane Hill, Hamilton, the Elsie Marian Carty Fund was founded. Mrs. Carty willed to the Institute a portion of her estate and a residuary interest therein to establish this Fund. It was her wish that the income should be used, primarily, for the assistance of promising research workers.

Since 1934 Mr. A. M. Nicholas has given an annual sum of £250 towards the salary of the Assistant Director.

This year the Carnegie Corporation of New York paid the travelling expenses of Dr. Feldberg, and are contributing in addition 4,500 dollars which, with £1,100 collected by Mr. Reuben Hallenstein, will be sufficient to support this worker for the next two years.

In addition, a number of smaller gifts have been received from time to time from trusts and private individuals.

The Institute is controlled by a Board consisting of representatives of the Walter and Eliza Hall Trust, of the University of Melbourne, and of the Committee of Management and Medical Staff of the Royal Melbourne Hospital. During the war years Professor Sir Harry Allen acted as Honorary Director. In 1919 Dr. S. W. Patterson was appointed first Director; in April, 1923, he resigned, and was succeeded by Dr. C. H. Kellaway in August, 1923. During the interval Mr. H. Dew acted as Director.

The Director's Seventeenth Annual Report

TO THE BOARD

OF THE

Walter and Eliza Hall Institute of Research

IN PATHOLOGY AND MEDICINE.

JULY, 1936.

The most important work of the Institute this year has been in Virus research. This is the second year of the three-year period during which this is being financed by grants from the Rockefeller Foundation and from the Health Department of the Commonwealth Government.

It is gratifying to report that we have secured, for a period of two years, the services of Dr. Wilhelm Feldberg, a distinguished worker in Physiology. This has been made possible by the generosity of the Carnegie Corporation of New York and of a number of private individuals in Melbourne and Sydney. Our special thanks are due to Mr. Reuben Hallenstein, who contributed largely himself and commended the project to his friends.

Mr. Arthur Baillieu, the Chairman of the Board, went abroad on 25th April, and during his absence the Committee of Management of the Royal Melbourne Hospital is represented on the Board by Sir William Brunton, the Senior Vice-President of the Hospital. Mr. A. M. Nicholas returned to Australia in December of last year, but, unfortunately, had to apply for further leave of absence to the end of 1936 on account of ill-health. Mr. Russell Grimwade, who had ably taken Mr. Nicholas' place for a year, had to go abroad early in January, and was not available for a further period. Dr. Priestley went to America in February, and in his absence Professor Copland, the acting Vice-Chancellor, has taken his place on the Board.

Staff of the Institute.

It gives us great pleasure to welcome Dr. Wilhelm Feldberg, who came to us in June from the National Institute of Medical

Research, where he has been working since he left Germany three years ago.

Dr. E. V. Keogh, of the Laboratories Division of the Commonwealth Health Service, is still attached to the Virus Department, though during the latter half of 1935 he was engaged for part of his time at the Commonwealth Serum Laboratories.

Miss Phyllis Rountree gave up her research fellowship in the Virus Department at the end of December, and has since gone to England to do further work.

Miss Mavis Freeman returned from England in December after spending fifteen months working at the Lister Institute, London. She was appointed as Research Fellow in the Virus Department in Miss Rountree's place in January of this year.

Miss E. Kennedy left us at Easter, and was married shortly afterwards. Miss Williams has taken charge of the Media Department.

Miss Cecily Timmins joined Dr. Burnet's department as a voluntary worker on 27th April.

We congratulate Mr. C. G. Setter, who has been Mr. Holden's personal assistant for eight years, on obtaining a free place at the University. Mr. Setter is doing a science course, but will continue his association with the Bio-chemical Department during the University vacations. In the Bio-chemical Department Mr. Holden has had some voluntary technical help. Miss L. Brien joined this department as a voluntary part-time technician in November, and Miss Marjorie Bick in February.

Department of Virus Research.

Psittacosis.—In the last Annual Report investigations were described which indicated that psittacosis was a very widespread disease of native Australian parrots, and it was suggested that human cases would probably be recognised in Australia if medical practitioners kept the condition in mind. This opinion has been substantiated by this year's experience, and about a dozen cases of proven or presumptive psittacosis in human beings have been detected in Victoria. For the recognition of these cases and for the opportunity to investigate them we are greatly indebted to medical practitioners in various parts of the State. Epidemiological investigations have been carried out by Dame Jean Connor, while the laboratory work has been done in the Institute under Dr. Burnet's direction.

From the epidemiological point of view conditions in Australia differ from those in any other country from which human cases of psittacosis have been reported. Here a large proportion of the parrots and cockatoos exposed for sale are young birds

recently caught in the wild. It is known that a high percentage of such birds are infected with a mild form of psittacosis before being caught. Normally the disease causes no symptoms, and probably most of the birds become non-infective by the time they are fully adult. Captive birds, however, are frequently kept under bad conditions. They are crowded together in inadequately lit and dirty cages, and supplied with insufficient food of poor quality. Our present experience indicates that under these circumstances, in cockatoos in particular, a flare up of latent psittacosis infection is liable to occur. The birds become obviously ill; they are inactive, exhibit wasting and diarrhoea, and eventually die. Sick recently-caught cockatoos were responsible for five serious human infections, from two of which the virus was isolated, and for a number of associated minor illnesses, which probably represented mild attacks of the disease. Most of these cases resulted from contact with cockatoos of one particular batch received from the country a few weeks before the onset of the first case. We were able to examine the remaining birds of the batch, all of which were heavily infected with psittacosis, and were obviously excreting large amounts of the virus. Some time later a freshly-caught batch of cockatoos from the same locality was examined. These, though the virus of psittacosis was not actually isolated from any of them, had enlarged spleens, and presented other evidence suggesting past infection.

Recently-caught birds, whose latent infection has been lit up during captivity, thus appear to represent an important source of danger in Australia. Two other serious human cases, both proved by positive mouse inoculation tests, appear to have been infected from aviary-bred budgerigars. We have had no opportunity to investigate the general incidence of psittacosis in the local breeding establishments, but there were infected birds in both the small non-commercial aviaries kept by these last two patients. Until further evidence is obtained, it seems reasonable to suppose that conditions here amongst aviary budgerigars are very similar to those obtaining in California, where a considerable proportion of the aviaries are infected with psittacosis, which is usually of a mild type.

The clinical features of the Victorian cases have been or will be described by the doctors responsible for their recognition and treatment. In general they conformed to the type seen elsewhere in regard to symptoms and course, and showed the same characteristic age incidence, all the seriously ill patients being middle-aged or elderly. There were no deaths, but seven patients required hospital treatment, and at least three of these were gravely ill.

From these results it will be seen that psittacosis is a minor, but not insignificant, public health problem in Australia. Should it be considered of sufficient importance to call for official preventive action, the data obtained at this Institute during the last two years offer a foundation on which to base effective action.

Following the reports of Bedson, which emphasised its use in diagnosis, the complement-fixation reaction in psittacosis has been studied by Dr. E. V. Keogh. So far the results have been disappointing. Although a proportion of proven and suspected cases have given positive reactions, these have only been weakly positive. Two of the proved cases gave negative reactions. Attempts to increase the sensitivity of the test have resulted in false positives in control sera. This work is being continued, in the hope of increasing the sensitivity while retaining the specificity of the test.

Epidemic Influenza.

It has been established by Smith, Andrews and Laidlaw, at the National Institute of Medical Research, Hampstead, that some, at least, of the cases clinically diagnosed as influenza are due to infection by a virus with characteristic pathogenic effects on ferrets and mice. During June and July, 1935, there was a typical widespread prevalence of influenza in Melbourne, and it seemed important to see whether Australian infections of this type were due to the same virus as that isolated in England and America. Dr. Burnet found no difficulty in infecting ferrets with throat washings from a patient with a typical attack of uncomplicated influenza, and throughout the year under review has continued the study of the virus so obtained.

The Melbourne strain produces effects in ferrets and mice precisely similar to those described for English and American strains. In co-operation with the Hampstead workers, serological tests have shown that it is identical, or almost identical, with the classical WS strain isolated in England.

As soon as the strain had been established in ferrets and mice, attempts to propagate it on the chorioallantoic membrane of the developing egg were begun. For a considerable number of passages very little effect on the embryonic tissues could be seen, though multiplication of the virus was evidently occurring, since the egg material continued to be infective for ferrets and mice. Gradually the lesions on the egg membrane became more definite, and by the 40th passage they were unmistakable and constant. Since then there has been a steady and remarkable increase in the virulence of the virus for the embryo. Death of the embryo as a specific result of infection was first noted

at the 52nd passage between the third and fourth day after inoculation. By the 63rd passage death was occurring before the third day, and all the dead embryos were showing a striking haemorrhagic encephalitis, the cerebral ventricles being filled with blood and the brain tissue riddled with small haemorrhages. After the 70th passage all eggs opened 44 to 48 hours after inoculation were dead. The brain haemorrhages were still present, but were less massive, and in addition there were numerous haemorrhages in the skeletal muscles and occasional haemorrhage in the heart and gizzard. The most recent development noted at the 76th passage has been the appearance of skin haemorrhages, particularly in the feather follicles. In such eggs the lesions could hardly be distinguished from those of Newcastle disease virus.

Along with this development of pathogenicity for the embryo the membrane lesions have become larger and more constant in number and character. Their optimal development was reached between the 60th and 70th passages. Subsequent to this, the early death of the eggs did not allow sufficient time for the full development of the focal lesions. The egg passage virus can be very satisfactorily titrated by the pock-counting method and a variety of immunological work is in progress along these lines. Some reference to this is made in a later section of this report.

In addition to the purely experimental egg membrane work which has been described, clinical research on influenza is being undertaken in collaboration with Dr. Ian Wood and Dr. J. M. Andrew, and, with the co-operation of the authorities of the Children's Hospital, Melbourne, and of the Yallourn Medical and Hospital Society. The objective is to use the serum neutralisation test as a means of establishing what clinical types of febrile illness are actually caused by the influenza virus. Some interesting data have been already obtained, but it will need at least a year's experience before any conclusions may be usefully drawn. A complementary series of studies is being made on the changes in antibody titre to influenza virus in the blood of a small selected group of normal individuals. Similar studies are being made in other countries, and it is only by the steady accumulation of data from all available sources that the problems of human susceptibility and immunity to influenza will be solved.

The Use of the Developing Egg in Virus Research.

Experience with this technique has continued to provide new evidence of its value as a general method of virus research, and increasing use is being made of it in this laboratory. We are now using eggs at the rate of over 10,000 per annum, the increase being mainly due to the development of accurate titration

methods, which are applicable to a wide range of viruses. During the year the viruses of vaccinia, fowl-pox, Kikuth's canary disease, ectromelia, infectious laryngotracheitis of fowls and influenza have been shown to be capable of accurate titration on the egg membrane by workers in this department.

"Pock-counting" Titration Method.

When active strains of the viruses mentioned above are suitably diluted and tested by standardised methods on the chorioallantoic membrane the resulting lesions take the form of isolated pock-like foci whose appearance varies according to the virus used. When conditions are satisfactory, the number of foci produced from a given inoculum varies only over a fairly narrow range, and if different concentrations are used the number of foci is directly proportional to the concentration of virus. If one uses three eggs to each dilution tested, it is easily possible to distinguish two dilutions of virus, one of which is twice the concentration of the other. This is probably five times as accurate as any other current method of virus titration, and the accuracy of the method can be proportionally increased if larger numbers of eggs are used. Even if the egg method were no more accurate than the animal titrations ordinarily used, it would still present great advantages for such a laboratory as ours, where the animal supply and accommodation are limited.

In order to obtain satisfactory results in egg titrations, it is essential to determine the conditions in regard to the stage of development of the egg at the time of inoculation, the temperature of incubation and the duration of incubation after inoculation, which are optimal for the production of countable lesions with each virus. As a rule eggs inoculated at the 12th day of incubation provide the most suitable membranes. Some viruses, such as ectromelia and influenza, must be incubated at a low temperature, 36°-37° C., while fowl-pox and canary-pox viruses give better lesions at 39° C. In order to avoid difficulties due to the development of secondary foci, counts are usually made about 48 hours after inoculation, i.e., before the foci are fully developed. With those viruses which very rarely give secondary foci, such as laryngotracheitis and fowl-pox, more easily counted membranes may be obtained if they are allowed to incubate for a further 24 hours. Appropriate antisera will reduce the numbers of foci appearing with a given amount of virus.

Infectious Laryngotracheitis of Fowls.

It was mentioned in the last report that the method of propagation on the chorio-allantoic membrane had been used to assist in the diagnosis of certain outbreaks of disease in

poultry as due to the virus of infectious laryngotracheitis. With the co-operation of Dr. H. R. Seddon, Director of Veterinary Research in New South Wales, Dr. Burnet has made an extensive study of this virus, using the developing egg throughout as the "experimental animal." This work has resulted in the accumulation of a number of facts of practical importance for the control of the disease, but its chief value lies in the demonstration it affords of the applicability of the egg methods to virus problems.

It was known that after one attack of the disease fowls were immune to experimental infection with the virus, and that their sera contained virus-inactivating antibodies whose presence could be demonstrated by the usual titration methods in susceptible fowls. The first application of the quantitative egg technique was therefore directed toward demonstrating such antibody in the sera of convalescent birds. It was found that when virus was mixed with convalescent serum from an experimentally infected bird, the count of pocks developing on the egg membrane was only 0.1 to 1.0 per cent. of the control count in eggs inoculated with virus mixed with normal serum. The method, therefore, provided a "serum-neutralisation test," which could be applied to all the usual purposes subserved by such tests in virus work. The virus strains isolated from various outbreaks in New South Wales were shown to be serologically identical amongst themselves, and with a strain of American origin, thus finally establishing the Australian disease as the same as that originally described in America. Sera from all the recovered birds showed neutralising activity, but, in addition, a number of older birds not known to have been infected also showed similar antibodies. This probably indicated that subclinical infections with the virus had been occurring in New South Wales before the appearance of recognisable outbreaks.

Much more definite evidence of such subclinical infection was obtained from a study of the position in Victoria, where no recorded outbreaks have occurred. Through the help of Dr. H. E. Albiston and the Victorian Government Department of Agriculture, we were able to obtain material from the occasional sporadic cases of fowls dying with symptoms suggestive of infectious laryngotracheitis, and also a representative sample of fifty sera from older birds on ten different poultry farms. Most of the tracheal lesions examined have yielded no virus, but two birds obtained at different times from one farm both provided strains of virus similar to one another, but differing significantly from the strains responsible for typical epizootics. On the egg membrane they produce lesions without the central necrotic crater of the typical strains, and they are almost nonpathogenic when inoculated intratracheally into fowls

However, inoculated birds develop antibody in high concentration, and were immune to intratracheal inoculation with active strains of virus. When tests of the neutralising capacity of the 50 blood sera were made, it was found that only one farm gave samples all of which were free of antibody. All the other farms contained birds which had evidently at some time suffered a mild infection with the virus. From these two lines of evidence, it can be concluded that a mild form of laryngotracheitis infection is enzootic in most Victorian poultry farms, and that, under present conditions, it is unlikely that economically important outbreaks of the disease will occur. The suggestion has been made that the Victorian strain might prove a valuable immunising agent in regions where the epizootic form was causing serious losses, but no opportunity of testing this has yet arisen.

Nature of the Virus-antivirus Reaction.

The nature of the inactivation of laryngotracheitis virus by immune serum has also been studied. The results obtained were held to indicate that the virus-antivirus reaction differed in no essential respect from the well-studied bacteriophage-antiphage reaction, and in particular that they provided clear evidence that true *in vitro* union occurred between the two components. The nature of the virus-antivirus reaction has been a subject of considerable controversy during recent years. As it is one which is peculiarly suitable for study by the developing egg technique, quantitative investigation of three different viruses has been undertaken in regard to this point, of vaccinia by Dr. Keogh, and of laryngotracheitis and influenza by Dr. Burnet.

Dr. Keogh has found that the number of focal lesions produced by a vaccinia virus suspension on the membrane is proportional to the virus content of the inoculum, and that by this method vaccinia virus suspensions can be titrated to a high degree of accuracy. The effect of immune serum in reducing the number of lesions was studied in detail, and Dr. Burnet's results with the virus of laryngotracheitis were practically duplicated with vaccinia virus. It was shown that the virus particles unite with the inactivating principle of immune sera *in vitro*. There is a close similarity between the action of immune sera on vaccinia virus and on bacteriophage, and it is proposed to examine in some detail the bacteriophage-immune sera reactions, in the hope of elucidating the factors involved in similar reactions with viruses pathogenic for animals. Further work on the immunology of vaccinia is in progress.

Immunological studies of influenza virus using both mouse and egg titration methods are in active progress. It is already clear that a strong immune ferret serum produces typical

inactivation of the egg passage virus, and that the nature of the reaction is similar to that of other virus-antivirus reactions. Some human immune sera behave differently, showing far less activity when tested on the egg than when the usual mouse inoculation test is used. It is hoped to investigate the significance of this difference by utilising the clinical material referred to in a previous section.

Infectious Ectromelia of Mice.

Great difficulty was experienced in obtaining satisfactory results with the propagation of this virus in the egg until the influence of different temperatures had been investigated. It was then found that with eggs incubated constantly at the standard temperature of 39.5° C. no lesions were produced by the virus, though excellent results were obtained at 36-37° C. It was also found that changes, which were apparently seasonal, in the susceptibility of eggs made a great difference in the results. During the spring months, although fairly satisfactory results were obtained when mouse liver virus was inoculated on to the egg membrane, passage experiments usually failed and individual foci were badly developed. Both before and after this period, however, perfectly satisfactory results were obtained provided that the correct temperature of incubation was used, the virus behaving in every respect like such easily grown viruses as vaccinia and infectious laryngotracheitis. Titrations could be carried out by the pock-counting method with an equal degree of accuracy, and this method was used to demonstrate the presence of specific antibodies in the sera of immunised rats and mice.

The lesions of ectromelia on the egg membrane provide interesting histological material, the specific inclusion bodies developing early and providing an index of the spread of the virus through the various layers of the membrane. The influence of temperature can also be recognised histologically, membranes from eggs incubated near 39° C. showing much more efficient reaction against the virus, which is manifested by segregation and exfoliation of the infected and necrotic cells. At lower temperatures the infective process involves the whole thickness of the ectoderm, and specific inclusions may be found in the other layers. As is to be expected, the virus becomes generalised in these eggs, and death of the embryo results usually between the third and fourth days.

Fowl-Pox and Canary Virus.

Fowl-pox was the first virus to be grown on the chorioallantoic membrane by Woodruff and Goodpasture in 1931, and Kikuth's canary virus was shown to grow readily on the egg by Dr.

Burnet in 1932-33 at Hampstead. No attempt had, however, been made to use the egg method for quantitative work with these viruses. Kikuth's canary virus produces an acutely fatal disease of canaries, and the German investigators, who first described it, considered that it was closely related to fowl-plague. Burnet suggested that the virus was more akin to fowl-pox, and this view is now generally accepted. Since the two viruses attack quite different host species, it was difficult or impossible to apply the most important criterion of relationship, namely, the immunological one. With the development of egg titration methods applicable to both viruses, the study of their serological relationships was greatly simplified, and has been undertaken by Miss Lush. She has found that satisfactorily accurate titrations of the viruses can be made, and that antisera can be prepared. Fowl-pox antisera were made in the usual way by hyperimmunisation of fowls convalescent from the infection. The canary virus antiserum was obtained from a rabbit which had been immunised with large amounts of virus grown on the egg, and concentrated by prolonged centrifugation in the angle centrifuge. The results of cross neutralisation tests showed that each antiserum was active against both viruses, but that in each instance the neutralising power was greater against the homologous than against the heterologous virus. There was no cross reaction with either serum against vaccinia virus. It is therefore established that the canary virus of Kikuth belongs to the bird pox group.

Histology of Virus Lesions in the Egg.

Dr. Keogh is studying the histology of lesions producing vaccinia in the chorio-allantoic membrane, and, with Miss Lush, a similar study of fowl-pox and canary-pox is in progress.

The Entry of Viruses Into the Central Nervous System by the Olfactory Route.

Experiments by Dr. Burnet on infection of rats with louping ill virus by the intra-nasal route were described in the last report. These have been completed, and the results published. They showed that in this apparently insusceptible animal the virus ascended as far as the olfactory bulb, and multiplied therein, but did not further invade the central nervous system. Active immunity and the appearance of circulating antibodies were induced by these inapparent infections.

Tests of a number of other viruses showed that ectromelia virus inoculated intranasally in the rat also could be demonstrated later in the olfactory bulbs, and a study of this phenomenon was made by Miss Lush and Dr. Burnet. The results differed significantly from those obtained with louping

ill virus in that with ectromelia multiplication took place in the nasal mucosa, only small amounts leaking up into the olfactory bulb. Histological evidence of infection of the olfactory mucosa was obtained, and it was shown that circulating antibodies appeared after the infection. The only inoculated rat in which the virus failed to multiply in the nasal mucosa was one in which the olfactory apparatus was atrophic. The olfactory bulbs were extremely small; the olfactory mucosa was unpigmented, and on section the characteristic olfactory epithelium was absent. It was concluded that the point of entry and site of initial multiplication of the virus were provided by the specific olfactory cells. The importance of these cells as a portal of entry for a number of natural virus infections was suggested in the discussion of these experiments.

Louping Ill and X-disease.

Further attempts have been made to substantiate the hypothesis put forward two years ago in regard to the relationship of louping ill virus infection to the Australian epidemics of X-disease. Dame Jean Connor has been able to obtain sera from six reputed survivors of the 1917-1918 outbreaks. One of these sera, in four out of five tests, inactivated 10 to 100 minimal infective doses of louping ill virus, but the fifth test was negative, and a careful study of all the protocols indicated that to establish with certainty the significance of such very small amounts of antibody, impracticably large numbers of mice would be necessary. None of the other sera contained recognisable amounts of antibody.

If, according to the hypothesis, louping ill virus infection was in 1917-18 widely prevalent amongst sheep in western New South Wales, there should still be enzootic foci present. Dr. H. R. Seddon was good enough to co-operate in an attempt to find such foci by supplying sera from sheep from various parts of New South Wales where paralytic affections which might possibly represent louping ill virus infections were reported to occur. Thirty-four sheep sera were tested, in every case with negative results.

This year's experience renders it unlikely that any direct evidence of the nature of the virus responsible for the X-disease outbreaks can now be obtained. The circumstantial evidence put forward by Burnet in support of the louping ill hypothesis has recently been strengthened by the publication of comparative histological studies on X-disease material by Perdrau, and the hypothesis cannot be regarded as disproved by failure to obtain positive evidence eighteen years after the event.

Paralysis in Cats.

Dr. Keogh and Dame Jean Connor have done some further work on the nature of the disease causing paralysis in cats, observed during the field survey of the poliomyelitis epidemic at Camperdown last year. Emulsions of the cord of a cat observed at that time, which has been preserved in glycerine-ringer for some nine months, are still capable of infecting a proportion of cats inoculated. One of these inoculated cats showed post mortem findings typical of the abdominal form of feline distemper. Further study of this disease is deferred pending facilities for isolation and breeding a non-immune stock of cats. Meanwhile the virus is being maintained by occasional passage.

Bacteriophage Work.

A curious and rather striking example of apparent mutation in a bacteriophage was noted by Dr. Burnet and Miss McKie during their work with staphylococcal phages in 1930. The two mutants differ primarily in the appearance of their plaques, the original form producing a ring-shaped plaque with a heavy mass of secondary growth in the centre, while the variant produces a typical large clear plaque. Miss Lush has made a study of this phenomenon, and has obtained some unexpectedly interesting results. Briefly, the original race differs from ordinary phages mainly in the enormously greater ease with which it evokes the appearance of resistant variants. We have calculated that from 10 to 20 per cent. of effective contacts with bacteria of the susceptible strain induce change of the organism to the resistant form, instead of lysis. The variant, like any other normal phage, produces resistant forms with approximately 0.0001 per cent. of such contacts. The resistant strain appears very soon after contact with the phage, and is invariably lysogenic, i.e., filtrates from young broth cultures certain large amounts of phage of the original type. If, however, broth cultures of the lysogenic resistant strain are allowed to age for three or four days, filtrates are found to contain the more active variant phage. This phenomenon occurs regularly, and the induced active phage retains its new character indefinitely when propagated on the susceptible bacterium in the ordinary way. The investigation has provided two clearly demonstrable examples of induced but permanently inheritable changes in micro-organisms: (a) the induction of the resistant lysogenic variant bacterium by phage action; and (b) the change within the resistant organism from the original to the active variant type of phage.

Bacterial Polysaccharides and Bacteriophage Specificity.

It has been shown that to a large extent the range of bacteriophages which will attack a given strain of bacterium is determined by the nature of the bacterial polysaccharide antigen. Partially purified preparations of polysaccharide are capable of inhibiting the action of certain phages in a manner very comparable to the action of specific antiphage-sera. If we adopt the widely-held view that bacteriophages are in most respects closely akin to animal and plant viruses, a study of the phage-polysaccharide interaction may be expected to throw light on two of the most important theoretical problems of virus biology: (a) the basis of the specific virulence of viruses, in virtue of which they can infect only certain cell types in certain species, and (b) the nature of the virus-antivirus reaction.

Since her return from England, Miss Freeman has commenced work on this subject. So far the work has been mainly of a preliminary character, but some highly active preparations have been obtained, and she has been able to confirm most of the results described by Burnet and Gough in 1933.

Staphylococcal Toxins.

The observation recorded in the last Report that certain bovine strains of staphylococci produce only the B type of toxin has been extended during the year by Dr. Bryce and Miss Rountree. They have studied a large number of strains of staphylococci of various origins, and found that most bovine strains produce considerable amounts of B toxin, sometimes alone and sometimes in association with A toxin. A detailed study of the toxigenic power of one of the strains which produced only B showed that the conditions under which the toxin is produced are the same as are required for A toxin production. Pure B toxin was a satisfactory antigen, producing the corresponding antitoxin, which had no neutralising effect whatever on A toxin. By the action of formalin, the toxin could be converted into the non-toxic, but still antigenic toxoid. A few preliminary tests on sera from patients suffering from staphylococcal lesions of long duration showed that they might contain relatively large amounts of B antitoxin.

In the course of this work much use was made of sheep blood agar plates as a method of recognising the different toxigenic types of staphylococci. Characteristic appearances are shown by A, B and mixed toxigenic types in the form of haloes surrounding the colonies. This method made it much easier to look for evidence of dissociation of the common "mixed" types into pure A and B types. Miss Rountree found that with certain strains dissociation occurred readily, but that it was

difficult or impossible to retain on repeated subculture the capacity to produce only A or B toxin. Some apparently fixed variants were obtained, but most of the results suggested that for many strains the proportion of A and B toxins produced varies according to the rules which govern the alternation of H-antigens in the Salmonella group between specific and group phases. This appears to be the first recorded example of a dissociation process involving the production of antigenically distinct toxins.

F. M. Burnet:

"Enzootic Psittacosis amongst Wild Australian Parrots." "Journal of Hygiene," 1935, 35, 412.

"Inapparent Virus Infections (with special reference to Australian examples)." "British Medical Journal," 18th January, 1936.

"Inapparent Infection of the Rat with Louping Ill Virus." "Journal of Pathology and Bacteriology," 1936, 52, 213.

"Immunological Studies with the Virus of Infectious Laryngotracheitis of Fowls Using the Developing Egg Technique." "Journal of Experimental Medicine" (in the press).

"Influenza Virus Isolated from an Australian Epidemic." "Medical Journal of Australia," 9th November, 1935.

"Propagation of the Virus of Epidemic Influenza on the Developing Egg." "Medical Journal of Australia," 16th November, 1935.

"Observations on the Effect of Louping Ill Virus on the Developing Egg" (in the press).

"Influenza Virus on the Developing Egg. 1. Changes Associated with the Development of an Egg Passage Strain of Virus" (in the press).

F. M. Burnet and Dora Lush:

"Induced Lysogenicity and Mutation of Bacteriophage within Lysogenic Bacteria." "Australian Journal of Experimental Biology and Medical Science," 1936, 14, 27.

"Inapparent (Sub-clinical) Infection of the Rat with the Virus of Infectious Ectromelia of Mice." "Journal of Pathology and Bacteriology," 1936, 42, 469.

"The Propagation of the Virus of Infectious Ectromelia of Mice in the Developing Egg" (in the press).

"The Immunological Relationships Between Kikuth's Canary Virus and Fowlpox" (in the press).

F. M. Burnet and Jean MacNamara:

"Human Psittacosis in Australia" (in the press).

E. V. Keogh:

"The Titration of Vaccinia Suspensions on the Chorion-allantoic Membrane of the Chick Embryo, and its Application to Immunological Studies of Neuro-vaccinia" (in the press).

Lucy M. Bryce and Phyllis Rountree:

"The Production of B Staphylococcal Toxin" (in the press).

Phyllis Rountree:

"Preliminary Note on the Dissociation of Staphylococci into A and B Toxigenic Variants" (in the press).

The Bio-chemical Department.

Work on Snake Venoms.

Mr. H. F. Holden and Mr. C. G. Setter have studied the ultra-violet absorption spectra of a number of venoms from snakes of various countries. The venoms of seventeen species of vipers from North, Central and South America, from India and from Europe, and of fifteen species of colubrine snakes from India and from Australia were examined. The frequencies of maximal and minimal absorption and the specific absorption coefficients at these frequencies were determined. Differences in the absorption curves of the venoms could not be correlated either with known differences in their toxic activity nor with the biological classification of the species yielding them.

Mr. Holden has also investigated the changes in the absorption spectra of some Australian snake venoms in which the haemolysins had been inactivated by heat in acid or alkaline solution or by formalin. It appeared that inactivation by acid and by alkali involved different structural elements in the molecule in addition to those related to haemolytic activity. The results of haemolysis tests in the presence of lecithin suggested that two haemolytic factors were involved—one attacking the red blood cells directly, and one converting lecithin into a lysin. The absorption spectra of death adder venom fractionated with alcohol and of black snake venom which had been freed from its thrombin were also studied.

Studies on the ultraviolet absorption of haemoglobin and its various derivatives obtained from common domestic and laboratory animals are at present in progress in continuation of earlier published work with Professor Sir C. S. Hicks, of Adelaide.

This work has only been possible through the generous loan of a Hilger spectrograph and photometer from the Department of Physiology of the University by Professor W. A. Osborne.

Mr. Holden has spent several months on the careful investigation of the Cronin Lowe modification of the Bendien test for cancer, using an interferometer kindly lent us by the Commonwealth Serum Laboratories. Unhappily, this test has been found to give neither constant nor reliable results, and its further study has been abandoned.

Of the two new honorary technicians in this department, Miss Bick is studying protein coagulation by heat in an attempt to render Devot's method of determination more reliable for those proteins the coagulum from which tends to redissolve. Miss Brien is helping in the general work of the department, particularly in making up special reagents required in this and other departments of the Institute.

Publications.

Holden, H. F., and Setter, C. G.:

"The Ultraviolet Absorption Spectra of Snake Venoms." "Australian Journal of Experimental Biology and Medical Science," 1935, 13, 223.

Holden, H. F.:

"The Ultraviolet Absorption Spectra of Some Modified Snake Venoms" (in the press).

The Vaso-depressant Action of the Venom of the Australian Copperhead.

I have completed work on this venom which was commenced with Mr. Le Messurier in the early months of last year. The intravenous injection of a small dose of copperhead venom, or of other Australian venoms which are devoid of coagulant action, causes a significant but transient fall in blood pressure. After recovery from this, the animal no longer reacts to a second similar dose of venom, though it responds normally to other vaso-pressor or depressor substances.

This phenomenon was observed in a wide range of species. The fall of blood pressure is almost wholly due to peripheral and not to central action. The venom has no direct cardio-depressant effect—it is devoid of action on the carotid sinuses or upon the vagal endings. It has no significant immediate effect upon the pulmonary circulation. The fall of blood pressure is not related to the curari-like action of the venom nor is it a by-product of coagulative changes due to the presence of traces of thrombin. It occurs almost as strikingly in the fully atropinised animal, and full eserinisation does not affect it.

The stimulant action of the venom upon isolated plain muscle, the latent period observed when plain muscle is caused so to contract and the desensitisation to further treatment with venom which results, recall the anaphylatic reaction of sensitive plain muscle and suggest that the primary contraction might be brought about by the liberation of histamine.

This explanation might be held to account for the initial fall of blood pressure following the intravenous injection of venom, more particularly so since venom injected intravascularly causes an initial constriction of the vessels of the rabbit's ear and broncho-constriction in the lungs of the pithed guinea pig, in both cases with accompanying desensitisation to venom.

Against the hypothesis that histamine is liberated by the cytolytic action of venom is the regular fall of blood pressure which follows its injection intravenously in the rabbit anaesthetised with chloroform or ether, and the fact that we could not obtain direct evidence of the presence of histamine in perfusion fluid from isolated lungs of cats or in the thoracic duct lymph of dogs immediately following the intravascular injection of venom.

The tests for the presence of histamine in these experiments were made upon the isolated uteri of virgin guinea pigs desensitised with copperhead venom. These were then sensitive to doses of histamine of the order of 0.0003 m.g.

Though it is possible that some other histamine-like substance may be produced by the venom, it is more likely that its action is a direct one upon muscle or upon peripheral nerve endings, and that the latent period observed in the reactions is due to the slow diffusion of a toxic substance of relatively large molecular size.

Platypus Venom.

Mr. Le Messurier and I commenced this work early last year, using a sample of venom collected 40 years ago by Sir Charles Martin. Publication was delayed until a fresh specimen of venom was obtained in September last through the co-operation of Mr. F. Lewis, Chief Inspector of the State Fisheries and Game Department. We had hoped to ascertain whether there were any seasonal changes in the toxicity of the venom, but have been unsuccessful in an attempt made, with the co-operation of Mr. David Fleay at the Melbourne Zoological Gardens, to obtain venom from a living male platypus, and have so far only obtained one further specimen of venom from a freshly-dead animal.

The results of our experiments with Martin's sample of venom were described in last year's Report. Briefly, the venom has

feeble coagulant, haemolytic and cytolytic power, but no neurotoxic action. The most striking effect caused by intravenous injection is a fall of blood pressure which is probably the cause of the transitory shock-like condition which follows when the venom is so injected in unanaesthetised animals.

Wounds by the spur of the male platypus in man are attended by severe pain and symptoms of shock with local swelling and numbness in the region of the puncture. Following the subcutaneous injection of the venom in animals, there was no evidence of pain, but there was swelling at the site of the needle puncture, and the surrounding region became anaesthetic.

The fresh sample of venom was slightly more active in respect to coagulant action than our old mixed sample, which contained only traces of thrombin. The fresh sample also caused a fall of blood pressure when injected intravenously, but the old sample probably contained an additional vaso-depressor substance with a histamine-like action. With the fresh venom the initial injection appeared to desensitise the animal against the vaso-depressant action of venom subsequently injected.

C. H. Kellaway and D. H. Le Messurier:

> "The Vaso-Depressant Action of the Venom of the Australian Copperhead (*Denisonia superba*)." "The Australian Journal of Experimental Biology and Medical Science," 1936, 14, 57.
>
> "The Venom of the Platypus (*Ornithorhynchus anatinus*)." "The Australian Journal of Experimental Biology and Medical Science," 1935, 13, 205.

I have spent nearly three months this year as one of three "Organisers" whose function it was to report on the structural defects of the present Royal Melbourne Hospital and on the requirements of the proposed new hospital on the Parkville site.

During this period Mr. R. D. Wright, Honorary Outpatient Surgeon to the Royal Melbourne Hospital, and Senior Lecturer in Pathology at the University, has had full use of my laboratory and assistant. He has during this time carried out some interesting observations upon the effects of increased intracranial tension upon the vascular and respiratory systems.

This investigation showed that the effect of rising intracranial pressure is not one of obliteration of blood vessels but of reduction in the rate of flow of blood through them. The medullary centres are not so sensitive to oxygen lack as is usually taught, whereas the cardiovascular receptors are considerably more sensitive. Changes in respiration, blood pressure and pulse rate do not occur with rise of intracranial pressure until this is near the arterial blood pressure level.

The idea that the cranium is a rigid box with its vasculature contained in it needs modifying to this extent, that the great venous sinuses are not subjected to increased intracranial pressure, and are always in free communication with the outside vasculature.

R. D. Wright:

"Experimental Observations upon Increased Intracranial Pressure" (in the press).

Acute Anaemia Due to Haemorrhage.

Dr. Ian Wood, the Marion Carty Research Fellow, has been engaged for the last eighteen months studying the effects of severe haemorrhage, and especially the changes in the composition of the blood which accompany it.

Many patients suffering from critical loss of blood have been treated by the continuous drip transfusion of Marriott and Kekwick. For twenty-four hours, or even longer, blood from a series of donors has been forced into the veins of these patients, and often as many as five pints of blood have been administered. In all cases the beneficial effects of transfusion have been followed by estimations of the percentage of haemoglobin and of the amount of urea present in the blood.

The results of these tests have been found to be useful prognostic guides—a profound fall in haemoglobin percentage is attended and sometimes preceded by a rise in the blood urea, and the latter falls when the available haemoglobin is increased by transfusion.

Close co-operation between the staffs of the Hospital and Institute have been necessary in the many phases of this work, which has popularised the use of continuous transfusion in the Hospital.

Ian J. Wood:

"Some Observations on the Treatment of Haemorrhage" (in the press).

The Sterility of Catgut.

Miss F. E. Williams has continued her work on this subject, and has devoted special attention to the sterility of reagents used for the preparation, storage, and bacteriological testing of catgut.

It is essential to sterilise alcohol of all strengths which is used for these purposes. Of 64 strands of catgut, ten feet in length, which she sterilised by the iodine method recommended by Bulloch, using reagents whose sterility was impeccable, she found one strand only contaminated with a sporing organism.

Similar catgut prepared by the iodine method and stored in spirit not specially sterilised by filtration showed a high incidence of contamination when subjected to rigid bacteriological tests—four reels of fifteen tested being found to be infected with sporing organisms.

Miss Williams has also tested the sterility of tubed allegedly sterile catgut prepared by various manufacturers and sealed in glass. Of 126 tubes of plain catgut prepared by ten different firms, 44 were found to be contaminated with sporing organisms. Taking account only of the samples of these manufacturers whose products proved to be most reliable, approximately five per cent. of tubes were infected (three of 63 tubes).

Some of these tubes had been in the retailers' hands for some time, and of those of British manufacture some had not been passed under the catgut regulations of the Therapeutic Substances Act. Of the tubes supplied by British firms put on the market since these regulations were passed, 25 tubes were examined, and all proved to be sterile.

Of 76 tubes of chromic catgut manufactured by six different firms, 30 proved to be non-sterile, and of thirteen samples put on the market since the more rigid tests under the catgut regulations (1930) and the Therapeutic Substances Act, three were found to be infected.

Miss Williams has been able to put plain raw catgut through the sterilisation process, and test it for sterility by culturing in suitable media, resterilise and retest without impairing the tensile strength or the suitability of the catgut for surgical use. Catgut manufactured in Australia, both plain and chromic, has been tested after sterilisation by the iodine method and found to be very uniform in calibre and eminently suitable for surgical work.

F. Eleanor Williams:

"The Preparation and Testing of Surgical Catgut" (in the press).

Diagnostic Tests in Hydatid Disease.

Drs. Keith Fairley and Wright-Smith have analysed the results obtained until August, 1935, in testing patients by the intradermal injection of hydatid fluid. Only the immediate response was considered. Positive results were obtained in 76% of 135 patients tested before their first operation for hydatid disease. Of 33 patients with ruptured cysts, 31 gave a positive test, but eleven of nineteen patients with suppurating cysts of the liver failed to give an immediate reaction. The

introduction of more exacting standards for a positive reaction has reduced the proportion of cases of hydatid infestation in which the reaction is present before operation, but has also diminished the incidence of fallacious positive results. When the test is properly performed a positive immediate reaction correctly identifies the presence of hydatid infestation in about 90% cases. The greatest value of the immediate reaction is, however, in excluding hydatid disease. When there is no history of a recent urticarial rash the absence of an immediate response excludes a recently ruptured non-suppurating cyst.

Dr. Keith Fairley and Miss Williams have brought up to date the analysis of the results of complement fixation tests carried out in this Institute up to July, 1935. Of 207 patients tested before operation for hydatid disease, 109 (52.7%) gave positive results. Of 91 patients with residual or recurrent cysts, 52 (57%) gave positive results. Only about one in three of those with uncomplicated or degenerating cysts gave a positive result, though this was found in three-fourths of patients tested who had ruptured or suppurating cysts. The fixation of more than six M.H.D. of complement before operation suggests rupture or infection of the cyst. The same titre more than nine months after operation indicates that further active cysts are probably present. For diagnosis of hydatid infestation only positive results with this test are of value since negative results do not exclude hydatid disease. This test is especially useful in the diagnosis of recurrent or residual cysts, because in these conditions the intradermal reaction of Casoni is valueless.

Keith D. Fairley and R. J. Wright-Smith:

"The Intradermal Test in Hydatid Disease." "Royal Melbourne Hospital Clinical Reports," 1935, 6, 82.

Keith D. Fairley and F. Eleanor Williams:

"The Complement Fixation Test in Hydatid Disease," "Royal Melbourne Hospital Clinical Reports," 1935, 6, 73.

Bacteriology and Clinical Pathology Department.

The routine diagnostic work in bacteriology, haematology, serology and allergy has been carried out as hitherto. So great has been the demand for the various tests, especially in haematology, that it has not been possible to undertake any special investigations.

During the year 5,807 tests for 3,520 in-patients, 5,909 tests for 2,856 out-patients, and 3,209 serological tests have been performed.

Dr. John I. Hayward resigned from the position of Resident Clinical Pathologist in January, and Dr. Mary Heseltine was appointed for the ensuing twelve months.

Tuition was given to 59 fifth-year students. The amount of attention given to each individual student is felt to be inadequate, but is the best that can be given under prevailing conditions.

Miss Williams has again been responsible for hydatid complement fixation tests, and Dr. Wright-Smith for Casoni tests.

With Dr. Theo Frank, Dr. Gardner reported a case of unusual interest, one of monocytic leukaemia, of which less than 50 cases appear in the literature to date.

T. J. F. Frank and Hilda J. Gardner:

"Monocytic Leukaemia." "Royal Melbourne Hospital Clinical Reports," 1935, 6, 16.

Biochemistry and Basal Metabolism.

The work of these two departments is still in charge of Miss Splatt. There is an increasing amount of routine work, and it is difficult for the routine staff to find time for special investigations. Miss Verney South, who gave very valuable honorary service in this department last year, sailed for England in March, where she hopes to enlarge her experience in the Courtauld Institute at the Middlesex Hospital.

In a considerable number of renal cases we have added to the routine blood urea and urea concentration tests, the urea clearance test of Van Slyke and Foweather's modification.

The determination of basal metabolic rates by the Douglas bag and Haldane gas analysis method was compared by Dr. T. Frank and Miss Splatt with the values obtained by Dr. Frank with Reid and Gale's formula methods.

Electrocardiography.

During the year 650 electrocardiograms have been done. We have found the Matthews portable instrument, which was presented to the Hospital some years ago by the ladies of the Box Hill and Mont Albert Auxiliary, most convenient and economical, and Mr. Hughes, who is in charge, has used it exclusively.

Morbid Anatomy.

During the year 491 autopsies and 1025 biopsy examinations were performed. Miss Wischusen has done all the photography and photomicrography. The photographic equipment presented last year by the ladies of the Box Hill and Mont Albert Auxiliary has proved invaluable.

In September of last year a definite forward move was made in the investigation of the neuro-pathological material of this

Hospital. Dr. E. Graeme Robertson, who returned from England in May of that year to join the honorary staff, has taken up this branch of work, and already much valuable material has been available for investigation. Dr. J. Monahan Lewis has very kindly lent us a Microtome for this work.

Museum.

New specimens added include a mycotic intracranial aneurysm, glioma of the spinal cord, carcinoma of the pituitary, gonococcal endocarditis, secondary carcinoma of the spleen, and a luteal-cell carcinoma of the ovary. We are indebted to Dr. C. H. Mollison and Dr. R. W. Chambers for the gift of specimens.

Teaching.

This year I have been giving the elementary University lectures in biochemistry and physiology to Science, Agriculture and Dental students for Dr. Ivan Maxwell, who is spending most of the year abroad.

Mr. Holden has given an introductory course of lectures on science to massage students.

Dr. Wright-Smith has given the usual course of lectures in pathology to fourth-year students in January and February. He has also given the lectures on bacteriology to the student nurses in the Hospital. During the year he gave fortnightly demonstrations of recent specimens of pathological interest to the honorary staff.

The Library.

Our thanks for the gift of journals and books are due to the following:—L'Académie Royal de Medecine de Belgique; The Cancer Research Committee, Sydney; The Commonwealth Department of Health; The Council of Scientific and Industrial Research; Miss Danks; Mr. Dobell, F.R.S.; The Government Institute for Infectious Diseases of the Tokyo Imperial University; The London Hospital; The Medical Research Council; The Middlesex Hospital Medical School; New York State Department of Health, Division of Laboratories and Research; Dr. R. J. Wright-Smith; La Société Royale des Sciences Médicales; The South African Institute for Medical Research; The University of Harvard, Department of Tropical Medicine; The University of Pennsylvania, Department of Pathology; The University of Tomsk.

CHARLES H. KELLAWAY,
Director.

LIST OF SUBSCRIBERS TO THE PHYSIOLOGICAL RESEARCH FUND.

(Dr. Wilhelm Feldberg)

Davis Gelatine Company	£100
Executors and Trustees of the late Sidney Myer	100
Reuben Hallenstein, Esq.	100
E. Hallenstein, Esq.	50
Sir John Higgins	105
Burdett Laycock, Esq.	100
F. D. Michaelis, Esq.	100
E. N. Michaelis, Esq.	100
Mrs. Claire Michaelis	50
R. L. Michaelis, Esq.	25
Mrs. Brightie Phillips (Sydney)	100
Relief Fund for Expatriated Germans	178

Walter and Eliza Hall Institute of Research in Pathology and Medicine

FINANCIAL STATEMENT FOR THE YEAR ENDED 30th JUNE, 1936.

RECEIPTS.

To Balance brought forward from 30th June, 1935				£3,257	15	8
„ Trustees, Walter & Eliza Hall Trust	£3,200	0	0			
„ University of Melbourne	750	0	0			
„ Felton Bequest Committee	300	0	0			
„ A. M. Nicholas	250	0	0			
„ Trustees late Anthony Mackie	85	0	0			
„ Trustees late T. J. Sumner	10	0	0			
„ Johnson & Johnson Ltd.	21	0	0			
„ A. C. Holme	0	10	0			
„ State Accident Ins. Office	4	13	4			
„ Australian, New Zealand Assoc. for the Advancement of Science	7	0	0			
„ Refund, Postages	1	6	0			
„ Melbourne Hospital, Refund	167	5	7			
„ Fees Received and Proceeds of Materials Supplied	416	17	3			
„ Interest	83	8	3			
				5,297	0	5
				£8,554	16	1

EXPENDITURE.

By Salaries and Wages	£3,969	16	5			
„ Materials	317	18	3			
„ Apparatus	62	4	9			
„ Sundries	147	18	3			
„ Repairs to Apparatus	9	17	10			
„ Repairs to Buildings	7	11	3			
„ Publications	73	5	9			
„ Fittings and Equipment	14	5	4			
				£4,602	17	10
„ Bio-Chemical Department				392	9	1
„ Library Account				2	15	0
„ Balance—						
Investments	1,875	0	0			
Cash—Agent-General, London	54	9	5			
Secretary's Advance Account	100	0	0			
Bank of New South Wales	1,527	4	9			
				3,556	14	2
				£8,554	16	1

THE ELSIE MARION CARTY ACCOUNT.

To Balance brought forward from 30th June, 1935	£258	6	2	By Salaries	£150	0	0
„ Interest	14	0	0	„ Materials, etc.	11	4	4
				„ Balance, Bank of New South Wales	111	1	10
	£272	6	2		£272	6	2

BIO-CHEMICAL DEPARTMENT ACCOUNT.

To Interest transferred from Endowment Account	£405	3	3	By Salaries and Wages	£797	12	4
„ Transfer from Income Account	392	9	1				
	£797	12	4		£797	12	4

LIBRARY ACCOUNT

To Interest on Investments	£100	12	8	By Books, Journals and Bookbinding	£103	7	8
„ Transfer from Income Account	2	15	0				
	£103	7	8		£103	7	8

VIRUS ACCOUNT.

To Balance brought forward from 30th June, 1935	£61	18	6	By Salaries and Wages	£1,279	10	4
„ Commonwealth Government	1,000	0	0	„ Materials, Apparatus, Equipment, Sundries	902	2	7
„ Rockefeller Foundation	1,000	0	0				
„ T. Manifold	23	3	0				
„ Debit Balance	96	11	5				
	£2181	12	11		£2181	12	11

PHYSIOLOGICAL RESEARCH ACCOUNT.

To The Carnegie Corporation, New York	£505	13	9	By Salaries and Wages	£67	18	4
„ Sundry Donations	1,108	0	0	„ Apparatus	67	2	7
„ Interest	15	15	8	„ Equipment	12	8	0
				„ Sundries	3	5	11
					£150	14	10
				„ Balance, Bank of New South Wales	1,478	14	7
	£1,629	9	5		£1,629	9	5

ENDOWMENT FUNDS.

To Balance Bio-Chemical Endowment Fund	£8,591	10	3	By Investments	£14,846	1	0
„ Balance Elsie Marion Carty Fund	4,233	15	3	„ Bank of New South Wales	9	4	6
„ Balance Library Fund	2,030	0	0				
	£14,855	5	6		£14,855	5	6

I have examined the Books, Vouchers, and Securities of the Institute for the year ended 30th June, 1936, and I certify that in my opinion the Statements of Receipts and Expenditure are correct statements as revealed by the books of the Institute. I have obtained all the information and explanations I have required.

14th July, 1936.

W. M. JARVIE, F.C.A. (Aust.), Auditor.